Beckwith Wiedemann syndrome: first international consensus regarding diagnosis and clinical management.

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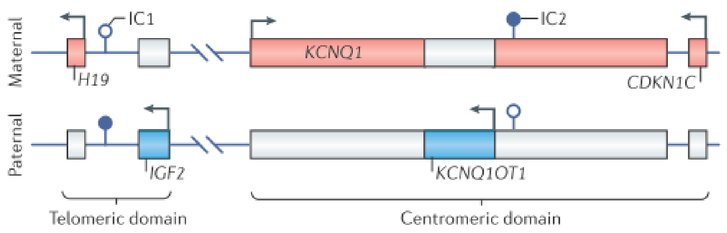
Introduction

Beckwith Wiedemann syndrome (BWS) is a rare overgrowth disorder associating macroglossia, exomphalos, lateralised overgrowth, organomegaly, hyperinsulinism, and an increased risk of embryonic tumor during early life. BWS is an imprinting disorder, with about 80% of children presenting a molecular defect (mostly a methylation defect at either ICR1 or ICR2, two differentially methylated regions, or paternal uniparental isodisomy) in the imprinted 11p15.5 region which contains the IGF2 and the *CDKN1C* genes.

To establish recommendations regarding clinical and molecular diagnosis of BWS, and clinical management of patients with BWS, and after a large review of the literature performed by a small group of international experts to establish a first draft document, a 3-day face-to-face meeting involving 35 participants was organized in March 2017 to discuss, formulate and vote on 72 consensus recommendations.



A new clinical scoring system

Cardinal features (2 points per feature)

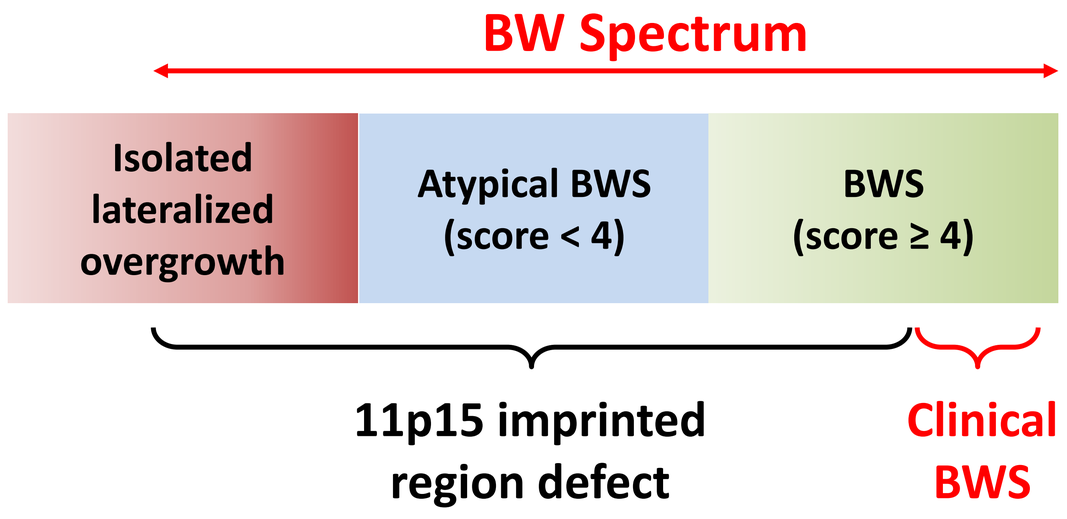
- Macroglossia
- Exomphalos
- Lateralized overgrowth
- Multifocal, bilateral Wilms tumour or nephroblastomatosis
- Hyperinsulinism (> 1 week and requiring escalated treatment)
- Pathology findings: adrenal cortex cytomegaly, placental mesenchymal dysplasia or pancreatic adenomatosis

Suggestive features (1 point per feature)

- Birth weight > 2SDS above the mean
- Facial naevus simplex
- Polyhydramnios and/or placentomegaly
- Ear creases and/or pits
- Transient hypoglycaemia (lasting < 1 week)
- Typical BWSp tumours (neuroblastoma, rhabdomyosarcoma, unilateral Wilms tumour, hepatoblastoma, adrenocortical carcinoma, phaeochromatosis)
- Nephromegaly and/or hepatomegaly
- Umbilical hernia and/or diastasis recti

≥ 2 points ⇒ Genetic testing

≥ 4 points ⇒ Classical BWS



A consensus for tumour screening... stratified according to the molecular defect

Molecular anomaly	Type of tumour	Protocol for tumour screening
IC 1 GOM	Wilms	Abdominal US scan /3 months until 7 years
IC2 LOM		No screening
UPD(11)pat	Wilms / Hepatobl.	Abdominal US scan /3 months until 7 years
Paternal dup.	Wilms / Hepatobl.	Abdominal US scan /3 months until 7 years
CDKN1C mut.	Neurobl.	Abdominal US scan /3 months until 7 years
Clinical BWS	Wilms	Abdominal US scan /3 months until 7 years

Ref: Brioude et al., Net Rev Endocrinol 2018

CONSENSUS STATEMENT

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EXPERT CONSENSUS DOCUMENT

Clinical and molecular diagnosis, screening and management of Beckwith–Wiedemann syndrome: an international consensus statement